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ORIGINAL ARTICLE

Stem Cell-Derived Exosome Therapy for Dental Diseases: From Bench to Bed in Dentistry

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ABSTRACT
Stem cells are undifferentiated cells that have significant potential to regenerate missing tissues and living structures. Exosomes are a specific subgroup of extracellular vesicles that are recognized as important mediators of intercellular communication in the process of regeneration. They contribute to various pathways of physiological and pathological processes. Given the ability of exosomes to carry molecular cargos and transfer bioactive components, exosome-based disease diagnosis and therapeutics have been extensively studied over the past few decades. The present review highlights the emerging applications of exosomes as therapeutic agents in craniofacial and dental regenerative processes. In addition, the current challenges and future perspectives of exosomes in dental clinical applications are discussed.
Keywords: dentistry, stem cells, exosome, regeneration, periodontal.

INTRODUCTION
Stem cells are a population of undifferentiated cells with the potential to differentiate into new cells and regenerate missing tissues; therefore, they play an important role in the treatment of diseases. In the field of dentistry, the oral facial tissues are considered as the target for stem cell therapy. Numerous extraoral and intraoral stem cells are used to achieve optimal treatment results. The present narrative review elaborates the use of stem cell technologies for treating different dental disorders and diseases.

Considerable advancements in biotechnology have enabled the replacement of missing teeth of patients through various methodologies that involve regenerative dental treatments. These include advanced bioengineering techniques such as dental stem cell banking, which is still under research and may be available in the near future. Different types of stem cells are present in the body and may be categorized based on their parent tissue. Regarding stem cells harvested from the oral cavity and surrounding tissue, the organs and tissues primarily utilized in regenerative dental medicine are the temporomandibular joint condylar cartilage, tongue, salivary gland, and pulp tissues, and periodontal ligaments (Gao & Cao, 2020). These are considered the most suitable target cells for use in tissue regeneration. Severe cavities and root fractures may occur owing to multiple factors, such as tooth extraction. Stem cell engineering is a promising approach for regenerating lost dental anatomical structures such as large periodontal defects and achieving alveolar bone regeneration (Peng et. al, 2020). Exosomes are considered specialized mediators of intercellular communication. Exosomes play an important role in a diverse range of physical and physiological processes (Vizoso, Eiro, Cid, Schneider, & Perez-Fernandez, 2017). The importance of exosomes is based on specific specialized material that is present in the cells. The cargo molecules present in the exosomes play fundamental physiological roles. Exosomes are used as therapeutic agents in drug delivery, cancer treatment, regeneration, and control of microbial infections in the oral cavity.

Stem cell therapy involves guiding stem cells to differentiate into specific mature cells in the body. Limitations in the use of stem cells involve their sensitivity, extended growth and differentiating times, and the availability of donor stem cells. Owing to these limitations, other methods involving regenerative medicine need to be developed as alternative approaches for regenerative treatments. One such method is exosome therapy, which does not involve using donor cells from the target patients. Instead, exosomes are extracted from donated human mesenchymal stem cells (MSCs) and sterilized (Zhou et. al, 2020). Exosomes are extracellular vesicles that fuse with the cell via endocytosis and act as intercellular communicators. They play an integral role in maintaining health and causing diseases (Shi, Mao, & Liu, 2020).

Exosomes are lipid-enclosed extracellular vesicles containing various cargo materials such as proteins, DNA, and RNA molecules. The diameter of exosomes ranges from 30 to 150 nm. Exosomes are often used by cells to discard cellular debris. Exosomes can be used to replace stem cells when there are limitations to the use of stem cells for regenerative therapy as described in the above paragraph. The biological function and potential for exosome treatment are evaluated based on the specificity of oral stem cells. In tumor treatments, exosomes are used as delivery tools for genes and certain drugs. Exosome-mediated delivery is also a potent therapeutic method for the treatment of microbial diseases. With respect to the maintenance of tissue homeostasis, exosomes play an important role in wound healing, immunotherapy, and tissue engineering (Zhou et. al, 2020).

While experiments performed in rat models have demonstrated that stem cell-derived exosome treatment (SCDE) alleviates renal ischemia reperfusion, it has also been shown to increase angiogenesis and other risks. Nevertheless, there are numerous positive outcomes of it, some of which include the treatment of chronic dental and oral diseases such as, periodontitis, Sjögren's syndrome, and oral Lichen Planus (Xing et al., 2020). Furthermore, SCDE are used as markers for the diagnosis and treatment of dental diseases caused by microbes such as pulp necrosis and periodontitis. Various microbes are present in the oral cavity, including multiple aerobic, anaerobic, and facultative bacteria such as Fusobacterium and Treponema. These microbes grow in the oral cavity, and their long-term presence is detrimental to dental and periodontal health.

Importance of SCDE Therapy for Microbial Diseases in Dentistry: Tooth cells have limited ability to repair degenerated tissue following damage. Therefore, SCDE is the most suitable tool for treating dental and periodontal damage. This therapy is important in dentistry as its use in combination with bioengineering techniques can help treat cell and tissue damage and restore missing structures lost because of diseases. Exosomes play an important role in dental applications and as therapeutic agents. They provide insights on various stages of diseases.

Different biomarkers play important roles in the diagnosis of different diseases. Autoantigens such as Ro/SSA, La/SSB, and Sm are related to Sjögren’s syndrome and others such as DUSP1, H3F3A, IL1B, and IL8 are related to oral cancers. Exosomes play critical roles in each step of the metastatic cascade and hence, can potentially act as biomarkers for metastasis and different stages as well as types of such diseases. Furthermore, the importance of SCDE in dentistry is based on the transportation ability of certain agents to oral cells by exosomes. Therefore, exosomes are also considered important owing to their therapeutic potential. In addition, this technique is used to control and treat microbial infections (Gao & Cao, 2020) and promote bone regeneration through the regulation of ontogenesis. Different functional cargos that stimulate effective functioning are present in the bone microenvironment.

The dental pulp performs a wide range of physical and physiological functions. It is an inverted tissue and is vascularized to a significant extent. The dental pulp responds in the form of neuronal sensitivity and bacterial insult in response to injury; it also acts against microbial infections. The vitality of teeth is related to the strength of the dental pulp. If the dental pulp is decayed or depleted, the tooth strength decreases, which makes it susceptible to damage. Diseases such as the endodontic disease are the most common tooth disease caused by microbe-induced inflammation or infection. Stem cell-based techniques can be used to diagnose and treat dental diseases (McBride, et al., 2017). In recent years, exosomes have been used in stem cell therapy as tools for the treatment of different dental conditions, such as edema and inflammation. The unique anti-apoptotic properties of exosomes include activation of the immune response and suppression of inflammation. Based on this evidence, exosomes are considered effective tools for disease treatment in dentistry.

Isolation Methods of Exosomes for Dental Applications: Oral tissue cells, such as teeth pulp tissue and periodontal ligaments, are primary sources of exosomes. Currently, different methods for exosome isolation are used for obtaining optimal results. Typically, current methods that are used for isolation do not accurately differentiate between exosomes and extracellular vesicles and hence, efficient isolation methods need to be developed.

Stem cells are primarily isolated from oral tissue, human exfoliated deciduous teeth, the apical papilla, and periodontal ligament space. Oral cells are better candidates than other cell types for stem cell isolation. The activity of stem cells isolated from the oral cavity is also higher than that of other cells owing to the higher rate of proliferation and greater osteogenic potential. Exosomes can be isolated from both normal and odontogenic pulp.

Techniques for Improved Production of Antimicrobial Agents: Antibiotics and antimicrobial agents are commonly used to treat dental and periodontal diseases of microbial origin. Penicillins are among the most common antibiotics used, and they play a critical role in the control of oral bacterial infections. The oral cavity environment is highly suitable for bacterial growth (Peng et. al, 2020). However, bacterial accumulation in the oral cavity is detrimental to dental health. Additionally, oral infections or diseases are not restricted to certain age groups. Advancements in medicine and technology may help control microbial activity in the oral cavity.

Periodontal and dental diseases are multifactorial diseases. To control microbial activity, the constant flow of saliva from the host cell must be controlled. Additionally, a complex electrostatic mechanism that controls bacterial activity should be employed, as bacteria can be both hydrophilic and hydrophobic. The microflora present on healthy teeth differ from that present on diseased teeth. The shift in the microflora causes changes in the plaque composition, which is the basic principle of dental disease development. The use of antibacterial agents, whether local or systemic, in conjunction with the mechanical removal of plaque is the most effective strategy for controlling the action of microbes (Shi Y. S.-L., 2019).

Actinomycetes are associated with various health benefits. They are a source of secondary metabolites, including important antibacterial, antifungal, antiviral, and anticancer agents. The discovery of actinomycetes was a milestone in microbial research. They produce bioactive metabolites with potent antibacterial and antiviral functions. The materials used in dental fillings also have antiviral and antibacterial properties. This is ensured as bacterial growth can affect the fillings, which contain metals such as gold, amalgam, silver, iron, and copper. The basic mechanisms employed in most antimicrobial strategies are the inhibition of nucleic acid synthesis, cell signaling pathways, protein synthesis, and depolarization of the bacterial cell membrane. Different types of antimicrobials are used to control microbial activities. Different diseases are associated with the growth of microflora in the oral cavity. An individual with a strong oral system may be considered healthy. Different chemicals are also used to treat microbial infections (Spees, Lee, & Gregory, 2016).

Evaluation of the Effects of Stem Cell Exosomes on Pathogenic Microbes Using In Vitro and In Vivo Methods: Owing to the regenerative, antimicrobial, and immunomodulatory potentials of stem cells, different in vitro and in vivo models are being employed for the effective utilization of stem cells to replace damaged differentiated tissues.

Communication between a parasite and its host cell owing to the activation of the immune system aids immune evasion. Exosomes play a vital role in the spread of immune-related molecules and thus, in minimizing the spread of pathogens. Exosomes are produced by two different mechanisms involving the suppression of interleukin (IL)-33 release in an in vivo type 2 response (Shen, et al., 2021). IL-33 is downregulated in response to the secretions by nematode and other parasites. The transfer of small RNAs from nematodes enhances immunity. Trypanosoma cruzi promoted the production of immune regulatory molecules such as IL-4 and IL-10. The thymine response was induced because the molecules enhance functioning. The formation of bones, blood vessels, and spicules in vivo indicated that the coagulation of 3D printing poly-lactide 3 (D-PLA) is effectively promoted when these are implanted in the rat calvaria bone. Exosomes are considered important contributors to molecule recognition and communication in pulp tissue generation and cell differentiation (Huang, Narayanan, Alapati, & Ravindran, 2016).

Exosomes promote odontogenic differentiation. Vascularization effectively enhances the generation of dental pulp implanted in the tooth root (Huang, Narayanan, Alapati, & Ravindran, 2016). Cell exosomes and oral tissue stem cells are supportive tools in the diagnosis and treatment of different dental diseases as they enhance the regeneration of degenerative tissue and cells. Primarily, the odontoblasts move to the site of injury and differentiate into dental pulp cells. The migration of odontoblasts toward the site of injury aids their development.

The expression of RUNX2, DSP, and DMP1 is enhanced through mineralized nodules; exosomes are extracted from dental pulp stem cells, and lipopolysaccharide secretion is controlled and monitored through the proliferation and migration of stimulated stem cells (Cheng, Zhang, Wu, Cui, & Xu, 2017). Consequently, sialoprotein is produced and extracted from dental pulp stem cells. Experimental results provide evidence that gel foam combined with chitin can induce nerve regeneration. The in vivo application methodology differed from that used in vitro. The in vivo method involves direct communication, as the substance is dissolved and reaches the target cell in the injury site.

The potential biological effects of exosomes are observed by monitoring intervention factors that target the cell. The specific cell type response induced by the proteins, mRNAs, and micro RNAs carried by the exosomes can be determined based on the parental cell status. The modulation capacity of exosomes in Schwann cells helps modify and change the exosome cargo. However, before the type of therapeutic modulation is selected, it is necessary to determine the source and state of the exosome donor (Chen, Qu, Cheng, Chen, & Xian, 2019).

Evaluation of Stem Cell Techniques in Dentistry: To date, numerous stem cell-based technologies have been established; these involve the identification, separation, and culture of stem cells. Magnetic-activated cell sorting and fluorescence-activated cell sorting are the most common methods used for stem cell identification. Traditional culture techniques include the reprogramming of somatic cells to pluripotent cells sequentially under optimum culture conditions on a layer of extracellular matrix complexes and feeder cells (Adak, Mukherjee, & Sen, 2017). Stem cells are the most suitable treatment tools for dental injuries and other dental conditions. The tooth offers the maximum number of proliferative stem cells, which can be used for both dental and non-dental purposes for stem cell-based therapies, which can be utilized to treat different clinical conditions. For example, bone marrow stem cells and periosteum-derived stem cells are suitable for the growth of alveolar bone owing to their compatibility with the target tissue.

Dental stem cells can be isolated from teeth that are surgically detached or misplaced. Moreover, cells can also be extracted from the pulp of both mature and exfoliated teeth, the periodontal tendon connecting the tooth basis with the bone, the tips of emerging roots, and the tissue that connects the unerupted tooth. Dental pulp stem cells are the chief source of cells to overhaul and regenerate injured cells; these cells are first isolated from the third molar of mature individuals.

The types of stem cells include mature stem cells, embryonic germ cells, and embryonic stem cells. Adult stem cells are derived from mature tissues in which they are present. Stem cells are formed in the blastocyst and earlier stages, such as in five-day-old embryos. Moreover, they work as an overhauling tool for the replacement of a particular type of cells and sustain the turnover of regenerative tissue, such as intestinal tissue, skin, and blood. Developing germ cells are isolated from fetal tissue at an advanced stage of expansion.

Stem cells of various origins have different applications and are generally less potent than embryonic stem cells. MSCs play a crucial role in dentistry, as they may aid in the regeneration of important structures, such as dental pulp, periodontal ligaments, and bone. Bone regeneration is a critical issue related to tissue engineering applications (Young & Speight, 2021). Numerous stem cell techniques involve osseous renewal, as gingival connective tissues are recognized to have osteogenic strength and can help in bone regeneration in cases of mandibular flaws. Dental stem cells can also be used in clinical applications, such as bone regeneration, muscular dystrophy treatment, and brain tissue regeneration (Antebi et al, 2018). However, dental stem cell techniques also involve numerous challenges and have negative effects. In bone tissue engineering, numerous strategies are designed for tissue regeneration using stem cells and cell culture methods. The combination of collagen sponge support and dental tissue-derived MSCs can be used to correct individual maxillary bone defects. The molecular, functional, and physiological characteristics of stem cells change considerably during long-term cultures. These alterations include damage to normal functions, reduction in propagation potential, and the Hayflick limit for cellular aging.

Guidelines for Stem Cell Production in Clinical Settings: Stem cell-based bioengineering techniques are in demand by patients with various diseases. Currently, commercial clinics are advertising stem cell-based therapies globally. Numerous clinics offer stem cell-based interventions, as these do not require the collection of clinical samples (Ducret, et al., 2021). However, the clinical use of stem cells is prohibited unless the conditions for storage and usage are mentioned in detail, the composition, safety, and origin of the goods are provided and defined appropriately, and the safety and efficacy of the process are established. There are important clinical applications of SCDE therapy.

Exosomes have a unique signature formed by nucleic acids, lipids, and proteins that replicates the composition of the parent cells, which makes them suitable for use in cell-independent therapeutics. Exosomes derived from stem cells have garnered considerable attention owing to their antimicrobial, regenerative, and immunomodulatory functions. Bone marrow-derived stem cells have been used in clinical practice for several years (Cheng et. al 2017).

Stem cell-derived exosomes mimic the therapeutic benefits of their parent cells, and this helps them evade the limitations of parent cells, provides a method for transportation and storage of cellular cargo without the loss of stemness, and offers a secure substitute for stem cell-based therapy. There are numerous types of stem cells with unique characteristics that can be derived from oral tissues. Stem cells can serve as replacements for old cells, particularly in cases of cell loss and damage.

Stem cell therapy involves the use of innovative technologies in different clinical challenges. While regeneration commonly occurs in individuals, predictable and complete regeneration is an elusive clinical objective (Antebi et al, 2018). The technological challenges in stem cell therapy are related to cell manipulation, delivery systems, and scaffold tools. Exosome therapy has been developed to overcome the clinical challenges in stem cell-based therapy, which are usually related to resistance or rejection of cells and issues in stem cell administration. Dental tissues are rich sources of MSCs that can be used in different clinical applications, particularly in regenerative and immune treatments. The procedure for the storage of dental stem cells is based on the mechanism observed in the deciduous and wisdom teeth of patients and is referred to as dental stem cell banking. This method is used to determine the potential of dental stem cell-based reformative therapy. The tissues with stem cells can be cryopreserved for several years, and their reformative potential can be preserved. Dental stem cells are resistant and can be isolated from cryopreserved teeth or tissues for future reformative treatments.

Quality Control Measures in the Isolation of Stem Cells: The manufacturing and development of therapeutic stem cell products require stringent quality control measures to confirm the safety, quality, and identity of cells. The combined use of biomaterials and exosomes is one of the most important strategies in tissue engineering. Exosomes combine with proteins such as fibronectin and type I collagen, as they are capable of interacting with biomaterials (Sullivan, et al., 2018). Living cells cannot be sterilized; therefore, sterility is a critical factor in exosome delivery. Tests for the detection of fungal or bacterial strains are used to assess sterilization. Viral testing should also be performed before SCDE therapy. The tests performed include nucleic acid, hepatitis C, and hepatitis B tests.

Testing for the existence of re-scheming vectors is crucial, as the combination of trajectories in the host genome can lead to various issues. Hence, testing aids in improving precision and decreasing the probability of false-positive outcomes. Additionally, quantitative PCR is used for sequence-specific labeling. The evaluation of cell viability as well as the method for assessing the viability is crucial for delivering a consistent and appropriate number of cells to the patient. It is important to measure cell viability using the method of validation, in which evaluation is conducted in iPSC cultures 48 h after revival.

While the doubling time is not considered important, it provides critical information on the cells and confirms the genetic stability of the cells over time. There are numerous stages in the development cycle, and the ratios of passages depend on the doubling of the cell population. Potency, which is associated with the properties of therapeutic materials, is an important measure of the clinical potential of cells (De Sousa, et al., 2017). The risks associated with the insufficient regulation of iPSC potential include the lack of efficacy of products, improper functioning of the cells, and tissue chimerism. While undifferentiated and self-renewal cell markers are used as substitutes to measure pluripotency, there is a need for a functional test for pluripotency.

Both culture conditions and pluripotency can influence the differentiation potential of stem cells. Moreover, while the propensity of distinct cell lines for differentiation into various lineages can be reported for the sake of collecting data, it is not a crucial aspect. Gene expression based on molecular RNA arrangement may predict pluripotency, which is of commercial importance as well. It is important that stem cells have adequate stability, clinical effectiveness, safety, purity, and identity; these parameters are usually confirmed through quality regulation testing.

The clinical effectiveness, tumorigenicity, abnormal immune responses, endotoxin presence, and independence from microbial contamination are also tested. Cell identification can be performed based on an understanding of biochemistry, cytogenetics, and cell biology. Micro-medical insurance is evaluated for each product batch, which comprise sterility tests for fungi and bacteria

(Samsonraj, et al., 2017). Therapeutic cell products are also used for testing irregular immune responses, in which the potential stimulatory effects of the products on lymphocytes are tested.

Relation between Mortality and SCDE Therapy in Microbial Diseases: As shown in a previous study, approximately 30% of patients with gastric cancer underwent stem cell transplantation. However, these patients died within 8–9 months after the procedure. The leading cause of death in hospitals is sepsis, and the rate of mortality is as high as 30%–40% in different cases (Chan, et al., 2019). Sepsis is a life-threatening condition with high mortality and morbidity rates. Microbial infections can also cause sepsis, which involves a complex interplay between the components of the immune system and bacterial pathogens. The excessive induction of endogenous pro-inflammatory coagulation and cytokine pathways during the early phase of sepsis can have negative effects on patients.

Stem cells can alter the expression of specific genes, enhance pathogen clearance, and repair damaged tissues in sepsis. With the increase in the global population, the incidence of degenerative dental diseases is also increasing, and these diseases can occasionally lead to cancer (Chan, et al., 2019). Dental diseases can influence a broad range of human actions, such as breathing, speech, memory, movement, and balance. Oral diseases are known to be caused by a combination of environmental and genetic factors.

Moreover, the degeneration of oral tissues and cells is a common characteristic of dental diseases, and it affects numerous zones of the brain, such as the hippocampus and the cortical region. Stem cells can be used as strengthening agents in dental and periodontal diseases. However, the use of MSCs as therapeutic agents in sepsis has numerous limitations, including gene instability and challenges related to quality control.

Advancements in Exosome Therapy for Microbial Infections: Exosome therapy is a highly flexible and targeted treatment option for musculoskeletal wounds, chronic pain, and osteoarthritis. The natural progression of age, degenerative diseases, and genetic diseases can restrict cellular communication. Exosomes mediate infection by transferring pathogen-related factors and molecules. Exosomes can enter cells directly and act as carriers of genetic material and proteins to other cells (Gutierrez-Millan, Calvo Díaz, Lanao, & Colino, 2021). Exosomes also participate in the transfer of information via signaling molecules, with specific functions that control the cellular response.

Exosomes have a cup-like structure and can carry nucleic acids, proteins, and lipids. Exosomes function in three stages as they repair cells present in the treatment zones. They have also been shown to remain active for 8 months. Exosomes are innovative forms of “bioactive vesicles”; these vesicles also participate in receptor transfer, which is downregulated in mature erythrocytes. Exosome therapeutic products are controlled by the FDA, and their use for treating human diseases requires FDA approval. Exosome therapy can be used as a replacement to drug-based therapy, and it has significant applications in the field of medicine.

The immunomagnetic bead separation technique is an important clinical method. In this method, antigens are hardened on the substrate, antibodies are present in the supernatant, and the culture medium washes liberated antibodies. Moreover, the antibody is linked to a specific antigen labeled with fluorescein (Wang, et al., 2017). Micro-fluid technology is also used in exosome therapy; it uses the biochemical and physical characteristics of dense bodies for microscale analysis, detection, and separation. Tumor-targeted exosomes can be observed in the plasma using a microfluidic chip designed in a herringbone nano-pattern.

Exosomes are strengthening components that can restore cell structure in different parts the body. They increase intercellular communication and are critical for improving cellular characteristics. Exosomes contain approximately three times more growth factors than adult stem cells. Moreover, exosome therapy does not involve the use of donor cells; as these are obtained from individual MSCs. Exosomes contain micro-RNA, messenger RNA, and lipids, which can relay signals to proteins and cytokines.

There are numerous challenges in the clinical use of exosomes, as they may promote particular diseases by erroneously disrupting the transfer of cellular materials. Certain exosome products may be produced according to a specific, efficient process, whereas other products may be designed using a different process (Crenshaw, Sims, & Matthews, 2018). Exosome therapy is performed most frequently in casualties, as exosomes may cross the blood–brain barrier for maximum efficiency, and they have minimal chances of clumping. Conversely, stem cells are unique as they can differentiate into any cell type and act as basic structural units in growth and repair processes. Overall, exosomes are extracellular agents and are not restricted to stem cells.

DISCUSSION

The primary role of exosomes is mediating cellular communication. In this narrative review, the application of stem cell-derived exosome therapy for microbial diseases was explored. The importance of exosome therapy was discussed based on the ability of exosomes to repair and replace damaged tissue. Exosomes may be applied in immunotherapy, homeostasis, wound healing, and tissue culture. However, there are certain limitations to the use of exosomes, including contamination, ethical considerations, and mutagenic tumorigenicity. This technique is highly beneficial for tissue replacement and transplantation, as it increases the rate of transplantation in damaged tissue.

In this study, the use of different techniques for isolating active substances that help suppress the effects of microbial contaminants was reviewed. Stem cell-based therapeutic approaches are important in dentistry as oral cells can be best used for cell production and replacement. In addition, the different techniques for controlling antimicrobial infections and producing stem cells in clinical systems were discussed. Moreover, the different quality measures used in exosome therapy were addressed.

The mortality rate associated with the use of cell-derived exosomes in dentistry was discussed. Furthermore, the guidelines for the production and isolation of stem cells were discussed. For stem cell identification, different methods such as identification and separation are used, as exosomes are markers that play an important role in these processes. Damaged and affected teeth are mostly replaced using the technique. However, older techniques have been replaced with modern techniques such as stem cell-derived therapy, in which the objective is attained using the technology that is more refined.

The findings of the studies reviewed show that stem cell-derived therapy is an effective method for oral disease treatment. In addition, various techniques have been introduced for controlling active microbial infection. The ease of quality control and provision of standardized methods under appropriate regulatory protocols are the advantages of this method. In any treatment protocol, the associated mortality rate is highly influenced by the quality of the methods used. In the future, we can expect the development of more effective and advanced techniques for the efficient control, monitoring, and treatment of different diseases using stem cell-derived therapy.

Conflict of Interest: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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